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09/492,954	01/27/2000	Anna Marie Pyle	58077/JPW/JSG	1593

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EXAMINER
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GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Jeanine A Goldberg

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 3/25/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

☒ Information Disclosure Statement(s) (P.T.O. Form 1449 or P.T.O. Form 1449A)

☐ Other (P.T.O. Form 1449)

### **DETAILED ACTION**

1. This action is in response to the papers filed March 25, 2004. Currently, claims 1-8 are pending.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.
3. Any objections and rejections not reiterated below are hereby withdrawn.

### ***Drawings***

4. The drawings are acceptable.

### ***Information Disclosure Statement***

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5 and 7-8 are rejected under 35 U.S.C. 103 (a) over Shuman (Proc. Natl. Acad. Sci. USA, November 1992, Vol. 89, pages 10935-10939) in view of Bjornson et al. (Biochemistry, (1994). Vol. 33, pages 14306-14316) as evidenced by Stern et al. (US Pat. 5,712,096, January 1998) and Karn et al. (US Pat. 6,316,194, Nov, 2001).

Shuman teaches a method for detecting the release of a single-stranded RNA from an RNA duplex which comprise admixing an RNA helicase with the RNA duplex under conditions permitting the RNA duplex to unwind the RNA duplex and release single stranded RNA, wherein the RNA duplex comprises a first RNA having a label and a second RNA wherein the unwound single-stranded RNA released from the duplex is detected by gel electrophoresis (Page 10936, Col. 1, lines 1 8-29, and 40-52. and Figures 1-2). Shuman teaches a method, wherein ATP and a divalent cation is present (Methods Section. Enzyme Assays Subsection). Shuman teaches a method of

complies detecting whether the single-stranded RNA is released from the RNA duplex at predetermined time intervals, and detecting therefrom the rate of release of the single-stranded RNA from the RNA duplex (Results Section, Kinetics Subsection and Figure 2). Shuman teaches a method of determining whether a compound is capable of modulating the release of a single-stranded RNA from an RNA duplex (Results Section, Requirements of Helicase Activity Subsection).

Shuman does not teach the method, wherein the first label is capable of producing a luminescent energy pattern wherein the first RNA is present in the RNA duplex which differs from the luminescent energy pattern produced when the first RNA is not present in the RNA duplex, thereby detecting release of a single-stranded RNA from the RNA duplex.

Shuman does not teach the method, wherein the first label is present at the 5' end of the first RNA and the second label is attached to the 3' end of the second RNA and the luminescent energy pattern results from interaction of luminescent energy released from the first label with the second label.

However Bjornson et al. teach the method, wherein the first label is capable of producing a luminescent energy pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern produced when the first nucleotide is not present in the nucleotide duplex, thereby detecting release of a single-stranded nucleic acid from the nucleic acid duplex after admixing helicase (Abstract. and Results section). Moreover, Bjornson et al. teach several advantages of using a fluorescent based assay for kinetic studies in general and particularly for

mechanistic studies for helicase-catalyzed unwinding. Bjornson et al. teach the method, wherein the first label is present at the 5' end of the first nucleic acid and the second label is attached to the 3' end of the second nucleic acid and the luminescent energy pattern results from interaction of luminescent energy released from the first label with the second label. Materials and Methods Section, Preparation of DNA unwinding subsection, and Results section and Figure 1).

Further, Stern teaches labeling both the 5' and 3' end of RNA. Stern teaches the RNA termini with fluorescein phosphoramidites (3' labeling) or CPG (5' labeling) or the incorporation of fluorescent adenosine or cytosine nucleotides at specific positions internal in the RNA (col. 15, lines 15-20). Moreover, Karn teaches FRET labeling of RNA. Karn teaches that the target RNA may be fluorescently labeled at the 3' or 5' end of a strand within the target RNA or within the chain of the target RNA. Karn teaches an entire section of fluorescent labeling which includes labeling with 2 fluorescent groups with one group placed adjacent to the 5' end of the target RNA and a second fluorescent group placed adjacent to the 3' end of the target (col. 11-12).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have substituted and combined the method of Shuman in view of Bjornson. The ordinary artisan would have been motivated to have substituted the fluorescent labeling method of Bjornson for the radiolabeled method of Shuman. The ordinary artisan would have been motivated to have the first label that is capable of producing a luminescent energy pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern

produced when the first nucleotide is not present in the nucleotide duplex. thereby detecting release of a single-stranded nucleic acid from the duplex after admixing helicase of Bjornson et al in the method of Schuman. The art clearly teaches that ability to label both the 5' and 3' end of RNA as well as DNA. Bjornson specifically states, "we describe a fluorescence assay that can be used to monitor helicase-catalyzed unwinding of duplex DNA continuously in real time (Abstract, first sentence). The ordinary artisan would have been motivated to have used a continuously real time assay in lieu of a radiolabeled method without the functionality of real time detection. Further motivation is provided by Bjornson, "this emphasizes the utility of the continuous spectroscopic method described here, which allows many more time points to be collected, thus enabling more accurate determinations of the complete time course and observed rate constants for all phase of a multiphasic reaction (Page 1431 6, Column 1, last sentence of the second paragraph). An ordinary artisan would have been motivated to have substituted and combined the method, wherein the first label is capable of producing a luminescent energy pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern produced when the first nucleotide is not present in the nucleotide duplex, thereby detecting release of a single-stranded nucleic acid from the duplex after admixing helicase of Bjornson in the method of Schuman, in order to achieve the express advantages, as noted by Bjornson, of a fluorescence assay that can be used to monitor helicase-catalyzed unwinding of duplex nucleic acids continuously in real time and which emphasizes the utility of the continuous spectroscopic method described here

allowing many more time points to be collected, thus enabling more accurate determinations of the complete time course and observed rate constants for all phase of a multiphasic reaction.

### **Response to Arguments**

The response traverses the rejection. The response asserts that there would not be a reasonable expectation of success in using fluorescence-labeled RNA in place of radiolabeled RNA in the method of Shuman. The response first argues that the detection of very small amounts of radiolabeled RNA. This argument has been thoroughly reviewed, but is not found persuasive because the claims do not require that any particular quantity of label be required in the method. The response submits Freifelder as support for the lack of expectation of success in substituting radiolabeled RNA for fluorescent labeled. This argument has been thoroughly reviewed, but is not found persuasive because the method for combining the references need to be the one suggested by the applicant. The ordinary artisan may be motivated to have substituted the radiolabeled method of Shuman for the fluorescence assay of Bjornson for the benefit of continuous real time analysis. While applicant suggests that fluorescent molecule was less sensitive, the ordinary artisan may be willing to forgoe sensitivity for the expected benefit of real time analysis.

The response further argues that the art did not provide a reasonable expectation of success in producing a fluorescence-labeled RNA for use in a helicase assay. The response argues that the assay requires the detection of labeled RNA in the nanomolar or subnanomolar range. This argument has been thoroughly reviewed, but is not found



persuasive because the claims are not directed to any particular nanomolar or subnanomolar range.

It is noted that the rejection has been amended to further incorporate the state of the art illustrating that the art teaches numerous methods for labeling both ends of RNA. Therefore, applicant's arguments are moot with respect to this argument.

Thus for the reasons above and those already of record, the rejection is maintained.

8. Claim 6 is rejected under 35 U.S.C. 103 (a) over Shuman (Proc. Natl. Acad. Sci. USA, November 1992, Vol. 89, pages 10935-10939) in view of Bjornson et al. (Biochemistry, (1994), Vol. 33, pages 14306-14316) further in view of Nazarenko et al. (US Pat. 5,866,336, February 1999).

Neither Shuman nor Bjornson teach the labels fluorescein isothiocyanate and rhodamine isothiocyanate.

However, Nazarenko et al. (herein referred to as Nazarenko) teaches an extensive list of suitable moieties that can be selected as donor or acceptors in FRET pairs (col. 17-18).

It would have been prima facie obvious to a practitioner having ordinary skill in the art at the time the invention was made to have substituted and combined the labels fluorescein isothiocyanate and rhodamine isothiocyanate of Nazarenko in the method of Schuman in view of Bjornson. Bjornson teaches using fluorescein and hexachlorofluorescein which are among the listed donors and acceptors. Therefore, using alternative donors and/or acceptors which were known in the art would have the

ability to quench signals as the labels taught by Bjornson. Therefore, using equivalent labels in the method would have been obvious to the ordinary artisan. An ordinary artisan would have been motivated to substitute and combine the labels fluorescein isothiocyanate and rhodamine isothiocyanate of Nazarenko in the method of Schuman in view of Bjornson because Nazarenko teaches that the FRET donors and acceptors are functional equivalents.

9. Claims 1-3, 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eggleston (Nucleic Acids Research, Vol. 24, No. 7, pages 1179-1186, 1996).

Eggleston et al. (herein referred to as Eggleston) teaches a helicase assay based upon the displacement of fluorescent nucleic acid binding ligands. The helicase assay is continuous, kinetic assay based on the displacement of the fluorescent dyes from dsDNA upon DNA unwinding. Eggleston analyzes several dyes including ethidium bromide to function as suitable reporter molecules. Eggleston teaches that a variety of fluorophores were examined to determine their utility as reporter molecules in a continuous helicase assay. Reactions using several of these dyes share the properties of having relatively low fluorescence in the presence of ssDNA and significant fluorescence enhancement upon binding to dsDNA (page 1180, col. 2). Eggleston teaches that they anticipate that this dye displacement assay can find widespread use in the study of RNA helicases, thereby suggesting a reasonable expectation of success. Eggleston suggests that the dye displacement assay can be readily adapted for use

with other DNA helicases, with RNA helicases and with other enzymes that act on nucleic acids.

Eggleston teaches the details of the fluorometric helicase assay and how the assay was performed, measured and optimized depending upon the dye and enzyme concentration used (page 1181, col. 1). The unwinding was initiated by the addition of ATP in excess of  $Mg^{2+}$  ion concentrations (limitations of Claim 2, 8). As seen in the Figure 1, the nucleic acid is labeled at the 5' end. It is noted that the 5' end is not the 5' terminus. The 5' end is interpreted to mean nucleotides 5' of the middle of the nucleic acid (limitations of Claim 3). The assay is performed over a relative time, for example at 10 time intervals, see Figure 1 (limitations of Claim 7).

Eggleston teaches that H33258 displays the greatest dsDNA specificity relative to ssDNA followed by TO, EB and DAPI. Due to their specificity for dsDNA, strong fluorescence signal, and minimal fluorescence in the absence of DNA, the fluorophores DAPI, H33258 and TO were selected for further study.

Eggleston states that "the studies have focused on DNA helicases, but the dye displacement assay may provide a new means by which the unwinding activity of RNA helicases can be examined" (page 1185, col. 2). Eggleston teaches that "since this dye binds to RNA in addition to DNA, it is readily conceivable that RNA helicases may be amenable to this assay if an appropriate ligand, such as EB or perhaps, propidium iodide, is utilized" (page 1185, col. 2). Eggleston teaches that "once this parameter is optimized for a particular substrate and enzyme, the dye-displacement assay gives results which are consistent with those obtained from other types of assays" (page

1185). Therefore, while Eggleston's studies focus primarily on DNA helicases, Eggleston specifically teaches that the method would be applicable to RNA helicases and there would be a reasonable expectation of success for the RNA helicases method. Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have performed the dye-displacement assay using RNA helicase to analyze and study the continuous unwinding of RNA using the method taught by Eggleston.

10. Claims 1-3, 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kowalczykowski et al. (US Pat. 5,747,247, May 1998).

Kowalczykowski et al. (herein referred to as Kowalczykowski) teaches a helicase assay based upon the displacement of fluorescent nucleic acid binding ligands. The helicase assay is continuous, kinetic assay based on the displacement of the fluorescent dyes from dsDNA upon DNA unwinding. Kowalczykowski analyzes several dyes including ethidium bromide to function as suitable reporter molecules. Kowalczykowski teaches that a variety of fluorophores were examined to determine their utility as reporter molecules in a continuous helicase assay. Reactions using several of these dyes share the properties of having relatively low fluorescence in the presence of ssDNA and significant fluorescence enhancement upon binding to dsDNA (col 3, lines 30-45). Kowalczykowski teaches that they anticipate that this dye displacement assay can find widespread use in the study of RNA helicases, thereby suggesting a reasonable expectation of success. Kowalczykowski suggests that the

dye displacement assay can be readily adapted for use with other DNA helicases, with RNA helicases and with other enzymes that act on nucleic acids.

Kowalczykowski teaches the details of the fluorometric helicase assay and how the assay was performed, measured and optimized depending upon the dye and enzyme concentration used (col 7-8). The unwinding was initiated by the addition of ATP in excess of  $Mg^{2+}$  ion concentrations (limitations of Claim 2, 8). As seen in the Figure 1, the nucleic acid is labeled at the 5' end. It is noted that the 5' end is not the 5' terminus. The 5' end is interpreted to mean nucleotides 5' of the middle of the nucleic acid (limitations of Claim 3). The assay is performed over a relative time, for example at 10 time intervals, see Figure 1 (limitations of Claim 7).

Kowalczykowski teaches that H33258 displays the greatest dsDNA specificity relative to ssDNA followed by TO, EB and DAPI. Due to their specificity for dsDNA, strong fluorescence signal, and minimal fluorescence in the absence of DNA, the fluorophores DAPI, H33258 and TO were selected for further study.

Kowalczykowski states that "the dye displacement assay also provides a new means by which the unwinding activity of RNA helicases can be examined (col. 15, lines 4-5). Kowalczykowski teaches that "since this dye binds to RNA in addition to DNA, RNA helicases are likewise amenable to this assay if an appropriate ligand, such as EB or perhaps, propidium iodide, is utilized" (col. 15, lines 13-15). Kowalczykowski teaches that "the dye displacement assay can be adapted for use with any helicase, whether it utilizes a DNA or RNA substrate, provided that a suitable, minimally-inhibitory nucleic acid binding dye is selected" (col. 15, lines 15-20). Therefore, while Kowalczykowski's

studies focus primarily on DNA helicases, Kowalczykowski specifically teaches that the method would be applicable to RNA helicases and there would be a reasonable expectation of success for the RNA helicases method.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have performed the dye-displacement assay using RNA helicase to analyze and study the continuous unwinding of RNA using the method taught by Kowalczykowski.

11. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Eggleston (Nucleic Acids Research, Vol. 24, No. 7, pages 1179-1186, 1996) or Kowalczykowski et al. (US Pat. 5,747,247, May 1998) as applied to Claims 1-3, 7-8 above in view of Bjornson et al. (Biochemistry, (1994). Vol. 33, pages 14306-14316) as evidenced by Stern et al. (US Pat. 5,712,096, January 1998) and Karn et al. (US Pat. 6,316,194, Nov, 2001).

Neither Eggleston or Kowalczykowski specifically teach using FRET methods for analyzing and monitoring RNA helicase.

However Bjornson et al. teach the method, wherein the first label is capable of producing a luminescent energy pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern produced when the first nucleotide is not present in the nucleotide duplex, thereby detecting release of a single-stranded nucleic acid from the nucleic acid duplex after admixing helicase (Abstract. and Results section). Moreover, Bjornson et al. teach several advantages of

using a fluorescent based assay for kinetic studies in general and particularly for mechanistic studies for helicase-catalyzed unwinding. Bjornson et al. teach the method, wherein the first label is present at the 5' end of the first nucleic acid and the second label is attached to the 3' end of the second nucleic acid and the luminescent energy pattern results from interaction of luminescent energy released from the first label with the second label. Materials and Methods Section, Preparation of DNA unwinding subsection, and Results section and Figure 1).

Further, Stern teaches labeling both the 5' and 3' end of RNA. Stern teaches the RNA termini with fluorescein phosphoramidites (3' labeling) or CPG (5' labeling) or the incorporation of fluorescent adenosine or cytosine nucleotides at specific positions internal in the RNA (col. 15, lines 15-20). Moreover, Karn teaches FRET labeling of RNA. Karn teaches that the target RNA may be fluorescently labeled at the 3' or 5' end of a strand within the target RNA or within the chain of the target RNA. Karn teaches an entire section of fluorescent labeling which includes labeling with 2 fluorescent groups with one group placed adjacent to the 5' end of the target RNA and a second fluorescent group placed adjacent to the 3' end of the target (col. 11-12).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have substituted and combined the method of Eggleston or Kowalczykowski in view of Bjornson. The ordinary artisan would have been motivated to have substituted the fluorescent labeling method of Bjornson for the radiolabeled method of Eggleston or Kowalczykowski. The ordinary artisan would have been motivated to have the first label that is capable of producing a luminescent energy

pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern produced when the first nucleotide is not present in the nucleotide duplex. thereby detecting release of a single-stranded nucleic acid from the duplex after admixing helicase of Bjornson et al in the method of Eggleston or Kowalczykowski. The art clearly teaches that ability to label both the 5' and 3' end of RNA as well as DNA. Bjornson specifically states, "we describe a fluorescence assay that can be used to monitor helicase-catalyzed unwinding of duplex DNA continuously in real time (Abstract, first sentence). The ordinary artisan would have been motivated to have used a continuously real time assay in lieu of a radiolabeled method without the functionality of real time detection.

Further motivation is provided by Bjornson, "this emphasizes the utility of the continuous spectroscopic method described here, which allows many more time points to be collected, thus enabling more accurate determinations of the complete time course and observed rate constants for all phase of a multiphasic reaction (Page 1431 6, Column 1, last sentence of the second paragraph). An ordinary artisan would have been motivated to have substituted and combined the method, wherein the first label is capable of producing a luminescent energy pattern wherein the first nucleotide is present in the nucleic acid duplex which differs from the luminescent energy pattern produced when the first nucleotide is not present in the nucleotide duplex, thereby detecting release of a single-stranded nucleic acid from the duplex after admixing helicase of Bjornson in the method of Eggleston or Kowalczykowski, in order to achieve the express advantages, as noted by Bjornson, of a fluorescence assay that can be



used to monitor helicase-catalyzed unwinding of duplex nucleic acids continuously in real time and which emphasizes the utility of the continuous spectroscopic method described here allowing many more time points to be collected, thus enabling more accurate determinations of the complete time course and observed rate constants for all phase of a multiphasic reaction.

12. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Eggleston (Nucleic Acids Research, Vol. 24, No. 7, pages 1179-1186, 1996) or Kowalczykowski et al. (US Pat. 5,747,247, May 1998) as applied to Claims 1-3, 7-8 above in view of Bjornson et al. (Biochemistry, (1994). Vol. 33, pages 14306-14316) as evidenced by Stern et al. (US Pat. 5,712,096, January 1998) and Karn et al. (US Pat. 6,316,194, Nov, 2001) in further view of Nazarenko et al. (US Pat. 5,866,336, February 1999).

Neither Eggleston or Kowalczykowski or Bjornson specifically teach using fluorescein isothiocyanate or rhodamine isothiocyanate.

However, Nazarenko et al. (herein referred to as Nazarenko) teaches an extensive list of suitable moieties that can be selected as donor or acceptors in FRET pairs (col. 17-18).

It would have been prima facie obvious to a practitioner having ordinary skill in the art at the time the invention was made to have substituted and combined the labels fluorescein isothiocyanate and rhodamine isothiocyanate of Nazarenko in the method of Eggleston or Kowalczykowski in view of Bjornson. Bjornson teaches using fluorescein

and hexachlorofluorescein which are among the listed donors and acceptors. Therefore, using alternative donors and/or acceptors which were known in the art would have the ability to quench signals as the labels taught by Bjornson. Therefore, using equivalent labels in the method would have been obvious to the ordinary artisan. An ordinary artisan would have been motivated to substitute and combine the labels fluorescein isothiocyanate and rhodamine isothiocyanate of Nazarenko in the method of Eggleston or Kowalczykowski in view of Bjornson because Nazarenko teaches that the FRET donors and acceptors are functional equivalents.

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

13. Claims 1-8 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-8 of copending Application No. 10/182,362. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims of the copending application and the instant claims appear to be identical in scope.

### ***Conclusion***

**14. No claims allowable over the art.**

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**Jeanine Goldberg**

**Patent Examiner**

April 27, 2004